PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

SECOND AND SUPPLEMENTARY NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION (TO DESIGNATED OFFICES WHICH APPLY THE 30 MONTH TIME LIMIT UNDER ARTICLE 22(1))

(PCT Rule 47.1(c))

To:

MILES, John
Eric Potter Clarkson
Park View House
58 The Ropewalk
Nottingham NG1 5DD
ROYAUME-UNI

RECORDS | CHECK
14 DEC 2005
PARTNER | ACTIONED

Date of mailing *(day/month/year)* 08 December 2005 (08.12.2005)	
Applicant's or agent's file reference RVCV/P31262PC	**IMPORTANT NOTICE**
International application No. PCT/GB2004/003386	International filing date *(day/month/year)* 05 August 2004 (05.08.2004)
Priority date *(day/month/year)* 05 August 2003 (05.08.2003)	
Applicant THE ROYAL VETERINARY COLLEGE et al	

1. **ATTENTION**: For any designated Office(s), for which the time limit under Article 22(1), as in force from 1 April 2002 (30 months from the priority date), **does not apply**, please see Form PCT/IB/308(First Notice) issued previously.

2. Notice is hereby given that the following designated Office(s), for which the time limit under Article 22(1), as in force from 1 April 2002, **does apply**, has/have requested that the communication of the international application, as provided for in Article 20, be effected under Rule 93*bis*.1. The International Bureau has effected that communication on the date indicated below:
17 February 2005 (17.02.2005)

AU, AZ, BY, CN, CO, DZ, EP, HU, KG, KP, KR, MD, MK, MZ, NA, RU, SY, TM, US

In accordance with Rule 47.1(c-*bis*)(i), those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

3. The following designated Offices, for which the time limit under Article 22(1), as in force from 1 April 2002, **does apply**, have not requested, as at the time of mailing of the present notice, that the communication of the international application be effected under Rule 93*bis*.1 :

AE, AG, AL, AM, AP, AT, BA, BB, BG, BR, BW, BZ, CA, CR, CU, CZ, DE, DK, DM, EA, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, SC, SD, SG, SK, SL, TJ, TN, TR, TT, UA, UZ, VC, VN, YU, ZA, ZW

In accordance with Rule 47.1(c-*bis*)(ii), those Offices accept the present notice as conclusive evidence that the Contracting State for which that Office acts as a designated Office does not require the furnishing, under Article 22, by the applicant of a copy of the international application.

4. **TIME LIMITS for entry into the national phase**

For the designated or elected Office(s) listed above, the applicable time limit for entering the national phase will, **subject to what is said in the following paragraph, be 30 MONTHS** from the priority date.

In practice, **time limits other than the 30-month time limit** will continue to apply, for various periods of time, in respect of certain of the designated or elected Office(s) listed above. For **regular updates on the applicable time limits** (30 or 31 months, or other time limit), Office by Office, refer to the *PCT Gazette*, the *PCT Newsletter* and the *PCT Applicant's Guide*, Volume II, National Chapters, all available from WIPO's Internet site, at http://www.wipo.int/pct/en/index.html.

It is the applicant's **sole responsibility** to monitor all these time limits.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.+41 22 740 14 35	Authorized officer Nora Lindner Facsimile No.+41 22 338 89 65

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
ERIC POTTER CLARKSON
Attn. Miles, John
Park View House
58 The Ropewalk
Nottingham NG1 5DD
UNITED KINGDOM

17 MAR 2005

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

	Date of mailing *(day/month/year)* 17/03/2005
Applicant's or agent's file reference RVCV/P31262PC	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/GB2004/003386	International filing date *(day/month/year)* 05/08/2004
Applicant THE ROYAL VETERINARY COLLEGE	

1. [x] The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

   When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

   Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Fascimile No.: (41–22) 740.14.35

   For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL–2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Müge Aydemir

(See notes on accompanying sheet)

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international pbulication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped),whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
RVCV/P31262PC		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB2004/003386	05/08/2004	05/08/2003
Applicant		
THE ROYAL VETERINARY COLLEGE		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      [ ] The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. [X] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box II).

3. [ ] **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      [ ] as suggested by the applicant.
      [ ] as selected by this Authority, because the applicant failed to suggest a figure.
      [ ] as selected by this Authority, because this figure better characterizes the invention.
   b. [X] none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2004/003386

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

   [X] a sequence listing

   [ ] table(s) related to the sequence listing

   b. format of material

   [X] in written format

   [X] in computer readable form

   c. time of filing/furnishing

   [ ] contained in the international application as filed

   [ ] filed together with the international application in computer readable form

   [X] furnished subsequently to this Authority for the purpose of search

2. [X] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB2004/003386

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/385 C12N15/62 G01N33/68 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C12N G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 2002/187131 A1 (DANIEL HAWIGER ET AL.) 12 December 2002 (2002-12-12) page 1, paragraph 8 page 2, paragraph 11 - paragraph 16 page 2, paragraph 19 - page 3, paragraph 21 page 3, paragraph 24 page 5, paragraph 45 - page 6, paragraph 50 page 6, paragraph 52 - paragraph 53 ----- -/--	1,2,4, 7-42,45 3,5,6, 43,44, 46-50

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
7 March 2005	17/03/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Montero Lopez, B

2

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	WO 03/040169 A (MEDAREX, INC.) 15 May 2003 (2003-05-15) page 2, line 5 - line 26 page 3, line 19 - line 24 page 5, line 1 - page 6, line 29 page 36, line 35 - page 39, line 37 page 67, line 25 - page 68, line 31	1,2,4, 7-42 3,5,6, 43-50
X Y	WO 01/64752 A (NEW YORK UNIVERSITY) 7 September 2001 (2001-09-07) page 6, line 5 - line 15 page 42, line 19 - page 43, line 22	41-44 3,5,6, 43,44
X Y	WO 02/20050 A (AKZO NOBEL N.V.) 14 March 2002 (2002-03-14) page 13, line 27 - page 14, line 15 page 16, line 3 - page 17, line 16	51 45-50
E	WO 2004/092195 A (ADMINISTRATORS OF THE TULANE EDUCATIONAL FUND) 28 October 2004 (2004-10-28) page 4, line 19 - page 5, line 2 page 9, line 22 - page 10, line 5 page 10, line 9 - line 18 page 21, line 14 - page 2, line 2; examples	1,2,4, 7-42

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2004/003386

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 22-29, 51, and claims 45 and 46, as far as encompassing an in vivo method, are directed to a method of treatment of the animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB2004/003386

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2002187131 A1	12-12-2002	US 2004258688 A1	23-12-2004
		AU 716056 B2	17-02-2000
		AU 4970296 A	21-08-1996
		CA 2211993 A1	08-08-1996
		EP 0808366 A1	26-11-1997
		JP 10513350 T	22-12-1998
		WO 9623882 A1	08-08-1996
WO 03040169 A	15-05-2003	US 2003031667 A1	13-02-2003
		CA 2466049 A1	15-05-2003
		EP 1448787 A2	25-08-2004
		WO 03040169 A2	15-05-2003
WO 0164752 A	07-09-2001	US 6391567 B1	21-05-2002
		AU 3992101 A	12-09-2001
		CA 2402054 A1	07-09-2001
		EP 1263789 A2	11-12-2002
		JP 2004536777 T	09-12-2004
		WO 0164752 A2	07-09-2001
		US 2003064071 A1	03-04-2003
WO 0220050 A	14-03-2002	US 6461616 B1	08-10-2002
		AU 8879401 A	22-03-2002
		WO 0220050 A2	14-03-2002
		US 2002155130 A1	24-10-2002
		US 2003026814 A1	06-02-2003
		US 2003021807 A1	30-01-2003
WO 2004092195 A	28-10-2004	WO 2004092195 A2	28-10-2004

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/003386	05.08.2004	05.08.2003

International Patent Classification (IPC) or both national classification and IPC
A61K39/385, C12N15/62, G01N33/68, C12Q1/68

Applicant
THE ROYAL VETERINARY COLLEGE

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Montero Lopez, B

Telephone No. +31 70 340-3739

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2004/003386

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 22-29, 51 and claims 45 and 46 as far as encompassing an in vivo method

because:

☒ the said international application, or the said claims Nos. 22-29, 51 and claims 45 and 46 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See separate sheet for further details

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	3, 5, 6, 9, 16, 17, 19, 39-50
	No:	Claims	1, 2, 4, 7, 8, 10-15, 18, 20-38, 51
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-51
Industrial applicability (IA)	Yes:	Claims	1-21, 30-50
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.

PCT/GB2004/003386

Re Item I
Basis of the report

1. Sequence listing pages 1-20 filed with the letter of 26.11.2004 do not form part of the application (Rule 13ter.1(f) PCT).

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 22-29, 51 and claims 45 and 46, as far as encompassing an in vivo method, relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

2. The claims relate to the use for vaccination of a compound comprising a moiety which selectively binds to a dendritic cell (HIV gp120, M. tuberculosis lam protein, Ebola virus glycoprotein) and an antigen. The application however, does not contain any technical evidence supporting the suitability of such a compound for vaccination. The examples provided are merely speculative and do not demonstrate that the aimed technical effect is achieved. Example 1 shows that HIV-1 gp120 binds DC-SIGN and states that gp120 is expressed together with model antigens (termed gp120-Ag). However, the result of examples 2-6 is not shown and only include speculative statements of the kind "it is expected" which do not constitute any evidence for the suitability of the claimed molecule for vaccination. Claims 1-51 are therefore not sufficiently supported by the description as requested by Article 5 PCT.

Re Item V
Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: US 2002/187131 A1 (DANIEL HAWIGER ET AL.) 12 December 2002 (2002-12-12)
D2: WO 01/64752 A (NEW YORK UNIVERSITY) 7 September 2001 (2001-09-07)
D3: WO 02/20050 A (AKZO NOBEL N.V.) 14 March 2002 (2002-03-14)

1. The underlying application relates to the use for vaccination of a compound comprising a moiety which selectively binds to a dendritic cell (HIV gp120, M. tuberculosis lam protein, Ebola virus glycoprotein) and an antigen.

2. Document D1 discloses a compound for delivery of an antigen to dendritic cells comprising a molecule binding to a dendritic cell receptor, such as DEC-205 and antigen (page 1, par. 8). Vaccination with various antigens is disclosed (page 2, par. 13-16). The endocytic receptor binding molecule is preferably an antibody which may be present with the antigen in a single polypeptide chain encoded by a polynucleotide molecule (page 2, par. 19 - page 3, par. 20). The compound can be used for vaccination of livestock animals (page 5, par. 46 and the examples). Claims 1, 2, 4, 7, 8, 10-15, 18, and 20-38 are therefore not novel and do not comply with the requirements of Article 33(2) PCT.

3. Dependent claims 9, 16, 17, 19 and 39-42, referring to trivial features such as the use of two antigens and an adjuvant or the recombinant production of the compound using a vector and a host cell, do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step. Therefore, the subject-matter of claims 9, 16, 17, 19 and 39-42 does not involve an inventive step in the sense of Article 33(3) PCT.

4. Claims 3, 5, 6, 43 and 44 specify the dendritic cell receptor as DC-SIGN and the binding moiety as HIV gp120, M. tuberculosis LAM protein or Ebola virus glycoprotein. Document D1 suggests in page 3, par. 22 that other receptors than DEC-205 can be used as targets for antigen delivery. In the light of the prior art the problem to be solved consists in providing an alternative receptor target for delivery of antigens to dendritic cells. Document D2 discloses that DC-SIGN is a receptor in dendritic cells for HIV gp120. It would be therefore obvious for the skilled person that the gp120 protein can be used as an equivalent to DEC-205 antibodies for targeting dendritic cells in a construct according to D1. Claims 3, 5, 6, 43 and 44 therefore do not involve an inventive step and do not comply

with the requirements of Article 33(3) PCT.

5. Claims 45-50 relate to a method and kit for determining wether an animal has been vaccinated with the compound of the invention by determining if it has an immune response to either the dendritic cell binding moiety or the antigen. This in itself constitutes a standard evident method for determining wether an animal has been administered a particular compound. Additionally, methods are available in the art to distinguish vaccinated animals from naturally infected animals, such as described in D3 (page 16, line 3 - page 17, line 16). Claims 45-50 are therefore not inventive and do not comply with the requirements of Article 33(3) PCT.

6. Claim 51 is broadly formulated as a method for vaccinating an animal which can be distinguished from a naturally infected animal. The expression "as described herein" is vague and unclear and does not convey any technical features to the claimed subject-matter. Therefore, in the light of D3 claim 51 is not novel and does not comply with the requirements of Article 33(2) PCT.

7. For the assessment of the present claims 1-14, 20, and 30-37 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
US2004/010832	28/10/2004	8/4/2004	9/4/2003

Re Item VII
Certain defects in the international application

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description, nor is this document identified therein.

2. The vague and imprecise statement in the description on page 26, lines 20-25 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.

Re Item VIII
Certain observations on the international application

1. Claims 1 and 42 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The functional statement "selectively binds to a dendritic cell" does not enable the skilled person to determine which technical features are necessary to perform the stated function.

2. Claim 1, directed to a compound for vaccination, contains a feature relating to the subject to be vaccinated (which moiety does not naturally occur in the animal). This renders the scope of the claim unclear, as a particular compound may or not be included in the scope of the claim depending on to which animal is administered (Article 6 PCT).

3. The relative term "naturally" in claim 1 is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear, Article 6 PCT.

4. The expression "pattern recognition receptor" used in claims 2 and 42 has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 84 EPC). A receptor is known in the art as recognizing one or several molecules. It is unclear what is meant under the word "pattern".

5. The terms "parts" in claims 5, 6, and 8-10, "variant" used in claims 8-10, and "portion" in claim 48 have no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 84 EPC). It is unclear what sort of variant (functional, structural) is meant and what the size and features of the "part" or "portion" should be.

6. The expression "molecule associated with a disease" used in claims 8 and 9 has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear, Article 6 PCT.

7. The expression "molecule associated with a disease" used in claims 8 and 9 has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear, Article 6 PCT.

8. The definition "OIE list A disease" used in claims 12, 26 and 34 has no well-recognised meaning and leaves the reader in doubt as to the identity of the diseases included in the scope of the claims, Article 6 PCT.

9. It is clear from the description that the feature of the combination of dendritic cell binding moiety and antigen is essential to the definition of the invention. Since independent claim 41 does not contain a feature directed to the antigen but only an insertion point for eventually inserting the antigen, it does not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.

10. Claims 48 and 49 are defined in terms of functional features ("which binds to an antibody raised against said moiety or antigen", "means for detecting an immune response") which do not enable the skilled person to determine which technical features are necessary to perform the stated function.

11. The relative terms "novel" and "described herein" used in claim 51 have no well-

recognised meaning and leave the reader in doubt as to the meaning of the technical features to which they refer, thereby rendering the definition of the subject-matter of said claim unclear, Article 6 PCT.